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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/547,995	10/28/2005	David John Grainger	50461/003001	8214

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
01/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/547,995	GRAINGER, DAVID JOHN	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16-41 and 43-49* is/are pending in the application.

4a) Of the above claim(s) *1-12,22-40,45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 16-21, 41, 43-44 and47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Newly submitted claims 17 and 47 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: n being defined as 9-12 as recited in claim 17 is distinct from the originally filed and examined n=8.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 17 and 47 are withdrawn from consideration as being directed to a non-elected species. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of the Claims

Claims 1-13, 16-41, 43-46 and new claims 47-49 are pending.

Claims 1-12, 22-40 and 45-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 14-15, 42 have been cancelled.

Claims 13, 16-21, 41, 43-44 and new claims 47-49 are under examination. (Please note the withdrawal of claims 17 and 47

from examination as being drawn to non-examined species as stated above).

Information Disclosure Statement

The information disclosure statement filed 9/7/2005 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

Applicants state that the references are listed in the enclosed Form PTO-1449 with the enclosed copies of the references. However, form PTO 1449 is not evident on file.

Response to Arguments

Applicant states that a copy of the IDS filed on September 7, 2005, which includes a Form PTO 1449 is submitted herewith.

Also enclosed is a Patent Office stamped return receipt postcard listing the IDS and Form PTO 1449. Applicant requests that the IDS be considered and that an initialed copy of the Form PTO 1449 be returned with the next Action in this case.

In reply, there is no Form PTO 1449 that accompanies the instant REMARKS or the stamped return receipt postcard listing the IDS and PTO form 1449. The PTO form 1449 on file does not list the references individually. It contains only the statement "International Preliminary Report on Patentability for PCT/GB2004/001016". 37 CFR 1.98(a)(1) requires a list of all patents, publications, applications, or other information submitted for consideration by the Office for compliance and consideration of the IDS.

Withdrawn Objection

In view of the new abstract submitted on 10/27/08, the objection to the specification is withdrawn. Also, in view of the amendments to the claims and applicant's arguments, the 35 USC 101 and 35 USC 112, new matter rejections are withdrawn. 35 USC 102 over Devlin rejection is also withdrawn in view of the amendments to the claims.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

A). Claims 13, 16-21, 41, 43-44, as amended and new claims 47-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antigenic amino acids selected from: GROUP 1 (charged) Arg, Lys, His, Asp, Gin; GROUP 2 (small hydrophobic) Gly, Ala, Leu, Ile, Val; GROUP 3 (large hydrophobic) Met, Phe, Pro, Tyr, Trp and GROUP 4 (hydrophilic) 8er, Thr, Asn, Gin, Cys (see e.g., page 55), does not reasonably provide enablement for X as groups of four of five or two groups of ten amino acids in any conceivable possible combinations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons as reiterated below.

The specification fails to teach how to make and use the claimed broad mixtures of peptides or library of mixtures wherein each of the amino acids in the mixtures comprised any of number of groups of amino acids. The claimed number of groups would encompass a huge combination of different amino acids in a group hence, a potentially huge numbers of mixtures of peptides. The specification recites the specific groups of e.g., hydrophobic

amino acids. However, the claimed groupings do not fall within the disclosed groups. Because peptide sequence hence, its conformation dictates the function of the peptide, it is not clearly apparent from the huge scope of the claims the ones that would result in a peptide having a function. Neither does it disclose a library that can be screened for a particular purpose/function. The high unpredictability in the peptide art is notoriously known in the art. The art is inherently unpredictable because it is not possible to predict which predetermined (variations) of amino acids would result in the desired mutant with a desired binding function. It is generally known that the conformational freedom that promotes binding, e.g., by modifying the peptides, might be restricted which may likely perturb the function and stability of the peptide (protein) in ways difficult to predict and measure. Some peptides accommodate variations at numerous sites throughout their primary sequence. Others are much less accommodating. It is difficult in general to predict which peptides are robust to variations, and which sites in a particular peptide are best suited to variations of multiple independent sequences. The complex spatial configuration of amino acid side chains in peptides and the interrelationship of different side chains in the randomized sites are insufficiently understood to allow for such predictions. Each of the 19 amino

acids is integrated at different frequencies due to the degeneration of the genetic code. For instance, serine is integrated six times more often than tryptophan, and three times more often than aspartic acid. It would therefore require an enormous effort to isolate mutants corresponding to amino acids represented only once or twice. Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined molecule in a peptide mixture that would result in a mutations having function without undue experimentation. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Response to Arguments

Applicant states that the specification clearly describes how to make the claimed libraries, including by use of standard solid-phase. peptide synthesis (see, e.g., page 22-28 and Example 4). Whether certain peptides within the libraries are not "functional" is not an issue, as any such peptides would simply not be recognized by an antibody within a test sample, and thus would be of no consequence. However, having a large

number of peptides with different sequences in a library will ensure that an optimal number of possible sequences within a given set of parameters are represented, to maximize antibody recognition and antigen identification.

In reply, Example 4 describes the method of making specific library and not the genus, containing numerous possible combinations, some of which or possibly all of the desired ones might not even be represented in the library. To make a library is known in the art. But the challenge still faced by skilled in the art is the screening of the huge collection of products such that the desired compound with the desired function is obtained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 16-21, 41, 43-44, as amended and new claims 47-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention, only for the maintained rejections as set forth below.

1-6. Withdrawn in view of applicant's amendments to claim 13 and arguments. However, please note that claim 18 has not been cancelled as argued.

7. Claims 41, 43-44 and 49 is indefinite as to the components of a kit such that the kit can be used for the intended purpose e.g., instructions as to the use of the kit.

Applicant submits that the claims are not indefinite, as they clearly set forth components that are comprised within the claimed kits.

In reply, the claimed kit only recites the components of a composition. This goes against the conventional wisdom in the art of a kit containing an instruction for the components to be of use.

A). Amended claim 18 and new claim 49 are indefinite in the recitation of the "library comprises mixtures representing all possible combinations of the groups", when e.g., there are only two groups.

B). Amended claim 41 is unclear as to the type or kind of "different" tag that can be attached to the different mixtures, especially in the absence of positive support in the

specification as to what is included or precluded by said different tag.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 13-21, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Houghten et al (Nature, 1991) for reasons of record as reiterated below.

Houghten et al discloses, throughout the article, at e.g., page 84 a mixtures of peptides and the heterogeneous libraries formed from the mixtures. The mixtures of peptide or library of hexapeptides comprises the formula as shown at Table 1, page 84, col. 2. See also, Fig. 1 at page 85 and Table 2 at page 86. Therefore, the specific mixtures of Houghten which describes specific residues fully meet the broad claimed mixtures/libraries with no defined structures or sequences.

Claims 13, 16-21, 41, 43-44 and 47-49 as amended and new claims 47-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Fowlkes et al (USP 6617114) for reasons of record as reiterated below. (Please note that amended, claim 17 and new claim 47 have not been examined as the new limitations i.e., the range 9-12 is different from the originally examined 8).

Fowlkes et al disclose throughout the patent, at e.g.,

col.16, line 46 up to col. 18, line 16:

> A peptide library is a combinatorial library, at least some of whose members are peptides having three or more amino acids connected via peptide bonds. In an oligopeptide library, the lengths of the peptides do not exceed 50 amino acids. The peptides may be linear, branched, or cyclic, and may include nonpeptidyl moieties. The amino acids are not limited to the naturally occurring amino acids.
> A biased peptide library is one in which one or more (but not all) residues of the peptides are constant residues. The individual members are referred to as peptide ligands (PL). In one embodiment, an internal residue is constant, so that the peptide sequence may be written as (Xaa)m-AA1-(Xaa)n…
> Where Xaa is either any naturally occurring amino acid, or any amino acid except cysteine, m and n are chosen independently from the range of 2 to 20, the Xaa may be the same or different, and AA1 is the same naturally occurring amino acid for all peptides in the library but may be any amino acid. Preferably, m and n are chosen independently from the range of 4 to 9.
> Preferably, AA1 is located at or near the center of the peptide. More preferably, AA1 is either (a) at least five residues from both ends of the peptide, or (b) is in the middle 50% of the peptide. More preferably, that m and n are not different by more than 2; most preferably m and n are equal. Even if the chosen AA1 is required (or at least permissive) of the TP binding activity one may need particular flanking residues to assure that it is properly positioned. If AA1 is more or less centrally located, the

library presents numerous alternative choices for the flanking residues. If AA1 is at an end, this flexibility is diminished. The most preferred libraries are those in which AA1 is tryptophan, proline or tyrosine. Second most preferred are those in which AA1 is phenylalanine, histidine, arginine, aspartate, leucine or isoleucine. Third most preferred are those in which AA is asparagine, serine, alanine or methionine. The least preferred choices are cysteine and glycine. These preferences are based on evaluation of the results of screening random peptide libraries for binding to many different TPs.
See further all the Examples which describe the specifics of the library containing tag.

Claims 41-44 drawn to a kit is disclosed at col. 31, line 15.

Fowlkes which describes specific residues for the library fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

Claims 13, 16-21, 41, 43-44, as amended and new claims 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Lynch et al (5962244).

Lynch discloses throughout the patent at e.g., col. 13, line 13 up to col. 14, line 67:

A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis, by combining a number of chemical "building blocks," such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide library, is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given

compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (see, e.g., U.S. Pat. No. 5,010,175, Furka, Int. J. Pept. Prot. Res., 37:487-493 (1991) and Houghton, et al., Nature, 354:84-88 (1991)). Other chemistries for generating chemical diversity libraries can also be used.

The invention provides compositions, kits and integrated systems for practicing the assays described herein. For example, an assay composition having a peptidyl-tRNA analog, an aminoacyl-tRNA analog, an immobilizable tag bound to the peptidyl-tRNA analog and a label bound to the aminoacyl-tRNA analog is provided by the present invention.

The invention also provides kits for practicing the peptidyl transferase screening assays described above. The kits can include any of the compositions noted above, and optionally further include additional components such as instructions to practice a high-throughput method of screening for a peptidyl transferase activity modulator, one or more containers or compartments (e.g., to hold peptidyl-tRNA analogs, uninoacyl-tRNA analogs, modulators, or the like), a control activity modulator, a robotic armature for mixing kit components, and the like.

Lynch which describes specific residues for the library

fully meet the broad claimed mixtures/libraries containing

any amino acid sequence.

Claims 13-21, as amended, new claims 47 and 48 and are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al (5858670).

Lam discloses throughout the patent at e.g., col. 3, line 14 up to col. 7, line 10:

> The present invention is directed to a library of bio-oligomers comprising all possible combinations of subunits…..FIG. 1. Scheme for random peptide synthesis using the split synthesis method for a random tripeptide with a terminal tryptophan added: X-X-X-W (wherein X=S, A, or V...).
> In specific examples... enzyme-chromogen labels and fluorescent (FITC) labels are used.

Lam which describes specific residues for the library fully meet the broad claimed mixtures/libraries containing any amino acid sequence.

Response to Arguments

Applicant submits that the claimed libraries are not completely random. Rather, the libraries are limited with respect to complexity, based on the requirement that the amino acids of the peptides of the mixtures be selected from particular groups of amino acids. The cited references describe libraries of peptides of including random amino acid sequences. In certain instances, particular positions of the peptides may be specified as having particular sequences, with the remaining being random, while in other

> instances, the lengths of the peptides are specified as being within particular ranges (see, e.g., the cited passages of Fowlkes). None of the references describes a library including mixtures of peptides characterized in that each position of the peptides is limited to a subset of the 20 naturally occurring amino acids (e.g., a subset of five or ten, as discussed above).

In reply, since applicant has combined all the separate rejections into one rebuttal hence, the response below will accordingly, treat the references collectively as one. Applicant’s arguments that the mixtures are selected from particular groups of amino acids are not commensurate in scope with the claims. The claims recite the 20 naturally occurring amino acids. The groupings of the 20 amino acids are not clearly set forth from the claim except for the phrase "combination of the four groups of five amino acids or the two groups of ten amino acids”. Because the claimed groups of five amino acids and two groups of ten amino acids are not positively recited or given in the specification or claim hence, the teachings of e.g., Lam or Houghten renders the claimed obvious. As read in light of the specification at e.g., paragraph [0130] which states:

> In such a mixture of peptides it is possible to specify that no amino acid is present in more than one of the groups

> of amino acids, i.e. that each amino acid will only appear when it's group is selected at a particular position. It is further possible to specify that each group of amino acids contains the same number of different amino acids. Thus for the twenty amino acids listed above, one could envisage dividing them into two groups of ten amino acids, four groups of five or five groups of four.

Accordingly, the broad claimed subset or subgroups of library can be readily envisaged from the specific subset of library of e.g., Lam or Houghten. The claim encompasses numerous possible combinations or possibilities as recited in e.g., claim 18.

Lam for example, recites at e.g., col. 9, line 5 -line 60:

> If the hexapeptide is to be comprised of five different amino acids, the method could be employed using five aliquots, each containing a different amino acid, at each coupling step. If, however, the hexapeptide is to be comprised of any of the basic set of twenty amino acids, the method could be employed using twenty aliquots at each coupling step.

> This method may be used for the synthesis of random peptides as well as for the synthesis of a peptide library that comprises **pre-determined sequences**. The synthesis of pre-determined sequences involves the use of specific...appropriately protected amino acids during specific coupling steps. For example, **one may select** amino acids at specific coupling steps such that the resulting peptides will have a probability or preference for a particular secondary structure, e.g. .beta.-sheet, .alpha.-helix, .beta.-turn, etc. For example, .alpha.-helix would be preferred **if Glu**, **Ala**, **Leu**, **His**, **Trp** are used as preferred amino acids; on the other hand .beta.-sheets would be preferred if Val, Ile, Tyr and Met are used. Alternatively, if **Gly**, **Asn**, **Ser**, **Pro**, **Asp** are used, a .beta.-turn structure would be preferred. Other examples

could be considered such as **acidic amino acids** near the N-terminal, and **basic amino acids** near the C-terminal, to stabilize an .alpha.-helix.

Furthermore, the disclosure of Fowlkes having the specified

range meets the claimed peptide with n=8.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 1-12, 22-40, 45-46 drawn to a non-elected invention nonelected. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/T. D. Wessendorf/

Primary Examiner, Art Unit 1639

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/547,995	GRAINGER, DAVID JOHN	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	